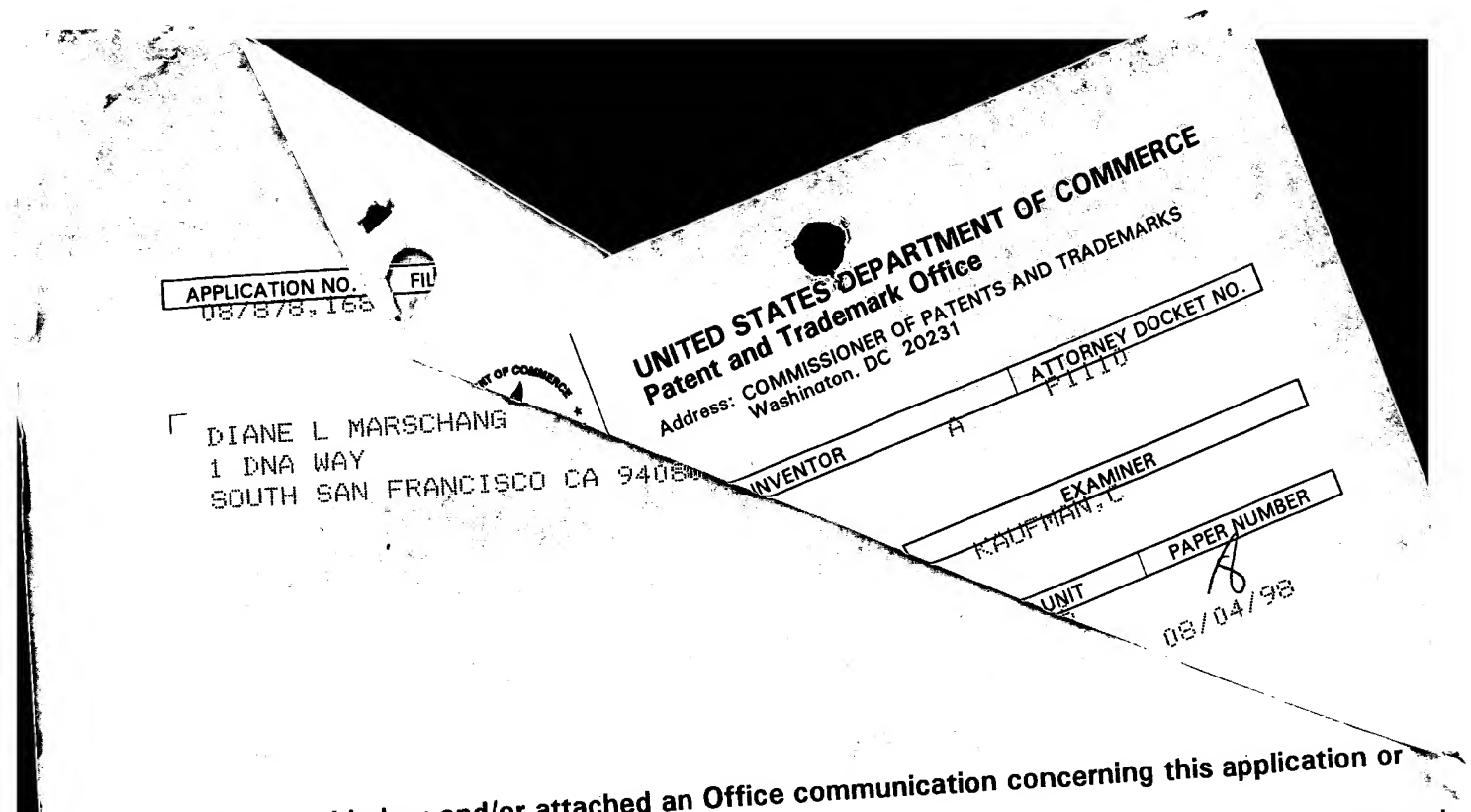

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1-File Copy

Office Action Summary	Application No. 08/878,168	Applicant(s) Ashkenazi et al.
	Examiner Claire M. Kaufman	Group Art Unit 1646

☒ Responsive to communication(s) filed on *Jun 18, 1997*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-29* is/are pending in the application.

Of the above, claim(s) *12-14, 22-25, 28, and 29* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-11, 15-21, 26, and 27* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-29* are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5 and 7*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The amendment filed 6/15/98 has been entered.

2. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1646.

Election/Restriction

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-11, 15-21, 26 and 27, drawn to Apo-2DcR polypeptide, chimeric polypeptide, article of manufacture comprising the polypeptide, nucleic acid, vector, host cell, and method of using the nucleic acid for polypeptide production, classified in class 435, subclass 69.1.

II. Claims 12-14, 26, and 27, drawn to antibody and article of manufacture comprising the antibody, classified in class 530, subclass 387.1.

III. Claims 22-23, drawn to transgenic animal, classified in class 800, subclass 2.

IV. Claims 24-25, drawn to knockout animal, classified in class 800, subclass 2.

V. Claims 28-29, drawn to method of modulating apoptosis, classified in class 514, subclass 12.

4. The inventions are distinct, each from the other because of the following reasons:

The polypeptides of Group I are related to the antibodies of Group II by virtue of being the cognate antigen, necessary for the production of the antibodies. Although the polypeptide and antibody are related due to the necessary stearic complementarity of the two, they are distinct inventions because they are structurally and functionally different, and the polypeptide can be used for another and materially different process other than for production of the antibody, such as in a

pharmaceutical composition in its own right, or to assay or purify the natural ligand of the polypeptide, or in assays for the identification of agonists or antagonists of the polypeptide.

The polypeptide and polynucleotide of Group I is related to the transgenic and knockout animals of Groups III-IV in that the animals expresses the polypeptide or have an altered gene encoding the polypeptide and because those animals express the nucleic acid or comprise an altered nucleic acid. Nevertheless, the inventions are distinct because the nucleic acid can be used for a materially different purpose such as for the *in vitro* production of the protein or for identification of related nucleic acids by hybridization screening. The inventions are further distinct because the polypeptide can be expressed by other means, for example by transfection of an *in vitro* host cell with the encoding nucleic acid. Also the polypeptide can be used for another and materially different process such as in the production of an antibody or affinity purification of the natural ligand of the polypeptide.

Inventions I and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide of invention I can be used in a materially different process such as in the production of an antibody or affinity purification of the natural ligand of the polypeptide.

The antibody of Invention II is unrelated to the transgenic or knockout animal of Inventions III-IV, as well as to the method of Invention V. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP § 806.04, MPEP § 808.01). In the instant case the antibody is structurally and functionally different than either animal and cannot be used in or produced by the method of Invention V.

The transgenic animal of Invention III is related to the knockout animal of Invention IV in that the transgenic expresses a non-altered or fully functional nucleic acid encoding the Apo-2DcR polypeptide, while the knockout animal has an altered gene and, in accordance with the art-accepted meaning of knockout, would not express a fully functional Apo-2DcR polypeptide. These animals have different functions and comprise different Apo nucleic acids.

The method of Invention V is unrelated to the transgenic or knockout animal of Inventions III-IV. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP § 806.04, MPEP § 808.01). In the instant case the animals cannot be used in or produced by the method of Invention V.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and because of their recognized divergent subject matter, and the search required for each Invention is not coextensive with another, restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Diane Marschang on June 11, 1998 a provisional election was made with traverse to prosecute Invention I, claims 1-11, 15-21, 26, and 27 as it relates to the polypeptide and not to the antibody. Affirmation of this election must be made by applicant in replying to this Office action. Claims 12-14, 22-25, 28-29, and also 26-27 as they relate to the antibody are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

6. The IDS submitted December 17, 1997 has been considered, but no references were found accompanying the IDS. Accordingly, with the exception of US Patent references 1-23 and references 179-180, the cited references were not available for consideration. Applicants may, in response to this action, submit copies of any references listed on the PTO 1449 which have not been considered. No fee or additional PTO 1449 is required with such a submission as it will be considered to have been part of the original IDS submitted prior to the first action on the merits.

Sequences

7. This application contains sequence disclosures that are encompassed by the definitions for nucleic and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth in the attached Notice to Comply with Requirements for Patent Applications Containing Nucleic Sequence and/or Amino Acid Sequence Disclosures. In the current application, the sequence in lines 1 and 3 of page 64 have apparently not been assigned sequence identifiers and, therefore, fail to comply with the requirements described above.

8. According to 37 CFR 1.821(d) (MPEP § 2422), where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. The sequences in lines 1 and 3 of page 64 must be assigned unique identifiers and be referred to with the appropriate SEQ ID NO.

Sequences Presented in Drawing Figures

9. 37 CFR 1.821(b) requires exclusive conformance, with regard to the manner in which the nucleotide and / or amino acid sequences are presented and described, with the sequence rules for all applications that include nucleotide and amino acid sequences that fall within the definitions. When a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either, in the drawing or in the Brief Description of the Drawings. (See MPEP 2422.02.) Figures 1A, 1B, 2, 8, and 9 show both nucleic acid and/or amino acid sequences. For each sequence present in a figure (amino acid sequences requiring different SEQ ID NOs than nucleic acid sequences), a unique sequence identifier must be used either in the figure or its Brief Description on page 10. Also, all references to a figure with a sequence must also use the sequence identifier (*e.g.*, p. 65, line 3).

Drawings

10. Figure 8 of the instant application is presented on two separate panels. 37 C.F.R. § 1.84 (u)(1) states that when partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. The two sheets must be identified by the same number followed by a capital letter. The two sheets of drawing which are labeled "Figure 8" in the instant specification should be renumbered "Figures 8A and 8B". Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84 (u)(1), Applicant is required to change the Brief Description of the Drawings and the rest of the specification accordingly.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-7, 16, 17, 19, 21, 26, 27 and dependent claims 8-11, 15, 18 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 are indefinite because it is not clear what range is encompassed by "about" 80 [or 90 or 95]%". The specification does not describe whether this term is intended to mean, for example, 79-100% or 60-100%.

Claims 1-3 are indefinite because it is unclear what is encompassed by the claims since the specification does not define how "identity" is to be calculated and the art has not recognized one way of calculating identity. While the specification says that gaps may be introduced and gives examples of computer software that can be used to calculate an alignment between sequences (p. 13, second ¶), it is not specified whether the results are reported relative to the query or matching sequence. Also, different computer programs given the same two sequences have been shown to produce different identity scores. Identity may be calculated relative to the query or matching sequence. These alternative means of calculating are important because they determines what, for example, 95% identity means. Consider two sequences: ACGTAC and ACAC. These can be compared in four ways. The example below illustrates how defining identity can influence the breadth encompassed by the claim. "Query" represents a single sequence being searched. "Match" represents a sequence found which matches the specific query.

match:	ACGTAC	4/6 = 67%	ACGTAC	2/6 = 33%
	| | | |		| |	
query:	AC - - AC	4/4 = 100%	ACAC	2/4 = 50%

Claims 1, 4-7, and 16-17 are indefinite because the significance of the parentheses around the SEQ ID NOs is not clear. This is particularly important in claim 7 in which the amino acid numbering is different in the figure (-40-259) and Sequence Listing (1-299). This rejection could

be obviated by eliminating reference to the Figure, therefore reciting only the SEQ ID NO, and for claim 7, changing the residues to 1 to 299 as they appear in SEQ ID NO:3.

Claim 19 is indefinite because it is unclear what the "control sequences" control. If the control sequences control expression, for example, the claim should say so.

Claim 21 is indefinite because there are insufficient method steps to practice the claimed invention so it is not clearly claimed. The step of culturing the host cell comprising the vector comprising an Apo-2DcR encoding nucleic acid linked to control sequences is not sufficient to effect production of Apo-2DcR polypeptide. If the host cell was cultured under conditions suitable for expression of Apo-2DcR polypeptide, and if a step such as 'expressing the nucleic acid molecule comprised by the vector' was added to the claim, the invention would be distinctly claimed.

Claim 26 is indefinite because it is unclear what the metes and bounds of "Apo-2DcR polypeptide". The specification says that this term include variants (p. 12, first ¶), and variants are about 80% identical to SEQ ID NO:1 and are agonistic or antagonistic modulators of apoptosis (p. 17, second ¶). Because it is not clear what 80% identical means (see paragraph third above this) and because the activity is represented by two opposite functions, what structures are encompassed by the claim is not clear.

Claim 26 is further indefinite because a composition must have two components and only one is listed, and also because it is unclear if the Apo-2DcR polypeptide is an active ingredient of the composition or merely present in trace amounts. Knowing whether the Apo-2DcR is critical to the composition is necessary to understand the breadth of the claim.

Claim 27 is indefinite became it is unclear if the instructions are intended to be further limiting to the article of manufacture, and if they are, what instructions they contain--*e.g.*, using the Apo-2DcR polypeptide as animal feed, for inhibition of apoptosis, and in the extreme--as a paper weight when amassed in sufficient volume.

Claim Objections

12. Claims 26 and 27 are objected to for including non-elected inventions.

Prior Art

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Wiley et al. (A) describe the cytokine TRAIL, also known as Apo-2 ligand, to which trail binding proteins like Apo-2DcR can bind.

14. The polypeptide and polynucleotide as claimed are free of the prior art of record.

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Friday from 8:00AM to 4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached at (703) 308-2731.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

cmk

July 22, 1998